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10/814,125	04/01/2004	Johan Frostegard	FROSTEGARD=1D	8029

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EXAMINER	
COOK, LISA V	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,125	FROSTEGARD, JOHAN	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 16-26* is/are rejected.

7)☒ Claim(s) *21-26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/720,967.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's response to the Office Action mailed June 12, 2006 is acknowledged (paper filed 12/5/06). In the amendments filed therein claims 1-14 and 16-20 were was modified. Claim 15 has been canceled. New claims 21-26 have been added. Currently claims 1-14 and 16-26 are pending and under consideration.

2. Objections and/or rejections of record not reiterated below have been withdrawn.

NEW GROUNDS OF REJECTIONS

Claim Objections

3. Claims 21-26 are objected to because of the following informalities: phosphochline is misspelled. The term should be spelled "phosphocholine". Appropriate correction is required.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of US Patent #6,780,605 as evidenced by Muzya et al. (Immunologiya, 1997, Vol:6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06).

The instant invention and US Patent #6,780,605 are drawn to methods of evaluating cardiovascular disease from the measurement of the presence and/or concentration of antibodies to PAF which includes antibodies to phosphocholine. Both methods used PAF as the antigen. See instant specification – page 10 for example. Muzya et al. are cited to show that antibodies binding to PAF by phosphocholine fragments (inherent feature of the method). See abstract. Thus the inventions read on the same scope measuring the same disorder (cardiovascular disease) and detecting the same antibodies (aPAF). Accordingly, the instant method is encompassed by the claims in US Patent #6,780,605.

6. Claims 14 and 16-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of US Patent #6,780,605 as evidenced by Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Abstract Only) and further in view of Baldo et al. (WO 87/05904).

Please see the discussion of US Patent #6,780,605 as evidenced by Muzya et al. and as set forth above.

Barquinero et al. as evidenced by Muzya et al. differ from the instant invention in not specifically teaching a means for testing comprising a ligand selected from the group consisting of phosphorylcholine and lysophosphatidylcholine.

However, Baldo et al. teach antigenic analogues of PAF (ligands) that are used to generate antibodies that bind PAF or antibodies to an antigen that binds aPAF. See claim 1 lines 6-7. The ligands including phosphorylcholine and is disclosed in the examples beginning at page 16 of the disclosure. Lysophosphatidylcholine structures are taught on page 30, for example.

The use of these ligands is taught to be useful because PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the ligand phosphorylcholine or lysophosphatidylcholine as taught by Baldo et al. in the measurements of antibodies to PAF and/or antibodies to an antigen(PAF) that binds aPAF as taught by Barquinero et al. as evidenced by Muzya et al. because Baldo et al. taught that PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

One of ordinary skill in the art would have been motivated to employ the cited ligands in order to produce sufficient amounts of PAF-antibodies for immunoassay testing.

Response to Arguments

Applicants have submitted a Terminal Disclaimer (TD) to obviate the ODP rejections, however the TD has been disapproved. Accordingly the ODP rejections are maintained.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 1-3, 6-8, 11-14, 16-17, 20-23, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988).

Muzya et al. teach that antibodies involving that bind to PAF, lyso-PAF, and acyl analogs of PAF. The binding of antiphosphatidylcholine antibodies to PAF and its structural analogs is related to the presence of phosphocholine fragments. The binding of antiphosphatidylcholine antibodies to PAF was exemplified in the sera of women with obstetrical-gynecological disorders (reading on spontaneous abortions). See abstract.

In particular, Muzya et al. teach an enzyme immunoassay (EIA) to study the binding of antibodies that bind to PAF and its structural analogues. In the assay PAF (a type of phosphocholine as exemplified in the specification on page 14 lines 12-11) was placed on polystyrene microplates.

The assay procedure also includes a reagent for detecting the antibodies bound to PAF (conjugates of murine monoclonal antibody with horseradish peroxidase IgM and IgG). See page 11, 2nd paragraph. The reagents are employed to measure PAF – antibody binding in blood serum test samples. The serum from a patient with late toxicosis in pregnancy had a high level of IgG antibodies that were reactive with PAF. The patient's serum bound significantly less to a PAF analogues. The researches taught that this may be caused by specific antibodies to PAF.

Although Muzya et al. teach the reagents and methods required by the claims; they do not specifically teach the diagnosis of risk of cardiovascular disease comprising atherosclerosis. In other words, Muzya et al. differ from the instant invention in not specifically teaching PAF as an indicator for cardiovascular diseases such as atherosclerosis via PAF quantification in serum and plasma.

However, Ostermann et al. teach PAF quantification in serum and plasma as well as its correlation/diagnosis (discrimination) in Atherosclerotic patients. See abstract and page 531 2nd paragraph. Thirty-Six health volunteers and 40 atherosclerotic patients were evaluated in the study. Blood samples were analyzed to determine PAF concentration.

The results showed a significant increase in serum PAF levels of patients suffering from coronary artery disease. Page 536, last paragraph. The researchers also measured plasma levels. See page 538.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure PAF concentrations in serum and plasma patients with cardiovascular disease such as atherosclerosis as taught by Ostermann et al. in the method of Muzya et al. because Ostermann et al. teach the critical role of PAF in myocardial infarction/atherosclerosis and its accuracy of correctly classifying subjects. See abstract. Ostermann et al. further teach that PAF could discriminate between low and high-risk groups and was an improvement over other commonly utilized discriminators (total cholesterol, VLDL/LDL-cholesterol, apo). See page 537 2nd paragraph.

One having ordinary skill in the art would have been motivated to do this because the early detection of such disorders is both beneficial in possible prevention and treatment of the disease.

II. Claims 4, 9, 18, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988) and further in view of Barquinero et al. (Lupus, 1994, 3, 55-58).

Please see Muzya et al. in view of Ostermann et al.

Muzya et al. in view of Ostermann et al. differ from the instant invention in not specifically teaching assay measurements by enzyme-linked immunoassay.

However, Barquinero et al. teach an ELISA assay to measure antibodies against platelet-activating factor (PAF) in patients with autoimmune diseases. Specifically blood sample from

patients with SLE (systemic lupus crythematosus), PAPS (antiphospholip syndrome), and syphilis. PAF was shown to be significantly present in patients with syphilis. See abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the reagents taught by Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11) in view of Ostermann et al. in an enzyme linked immunoassay (ELISA) as taught by Barquinero et al. (Lupus, 1994, 3, 55-58) because Barquinero et al. taught that the PAF ELISA could be used to detect syphilis. See Barquinero et al. abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF".

III. Claims 5, 10, 19, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988) and further in view of Smal et al. (Journal of Immunological Methods, Vol.128, 1990, pages 183-188).

Please see Muzya et al. in view of Ostermann et al.

Muzya et al. in view of Ostermann et al. differ from the instant invention in not specifically teaching assay measurements by radioimmunoassay.

However, Smal et al. teaches method to evaluate PAF in a specific and sensitive radioimmunoassay. In the procedure the anti-PAF antibodies showed specificity for the acetyl group at the C2 position of the PAF molecule and exhibited no significant cross-reactivity with

lyso-PAF or the naturally occurring lipids. The RIA was at least as good as the platelet-based assay for PAF but the RIA was simpler to perform, had higher capacity and did not have the draw backs of the inherent variability associated with the bioassay. See abstract and pages 186-187.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to take the reagents taught by Muzya et al. in view Ostermann et al. to measure PAF by radioimmunoassay procedures as exemplified by Smal et al. because Smal et al. taught that the RIA was at least as good as the platelet-based assay for PAF but the RIA was simpler to perform, had higher capacity and did not have the draw backs of the inherent variability associated with the bioassay. See abstract and pages 186-187.

Response to Arguments

8. Applicants arguments against the rejections of record are MOOT in light of the newly submitted claims. The rejections of record have been modified appropriately herein.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants contend that the reference of Barquinero et al. does not teach a correlation between anti-PAF antibodies and autoimmune disease. In fact, Barquinero provides a link between anti-PAF antibodies and syphilis. Further, Barquinero has been cited to merely teach

ELISA procedures for measuring PAF/anti-PAF binding procedures. This argument was carefully considered but not found persuasive because there is no requirement that the prior art must suggest that the claimed product (kit) will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. *In re Dillon*, 919 F.2d 688, 696, 16 USPQ 2d 1897, 1904 (Fed. Cir. 1990).

Applicant also contends that Muzya et al. only provide motivation to use phosphocholine as a ligand to detect antibodies to PAF, albeit in the context of gynecological disorders as opposed to CVD or syphilis. This argument was carefully considered but not found persuasive because Muzya et al. teach PAF measurement in various disorders/diseases taught by the prior art. See Muzya et al. page 9, 3rd paragraph – page 10, 1st paragraph. Further, an obviousness rejection is proper under Dillon so long as the prior art suggests a reason or provides motivation to make the claimed invention, even where the reason or motivation is different from that discovered by Applicant. *In re Dillon*, 919 F.2d 688, 696, 16 USPQ 2d 1897, 1904 (Fed. Cir. 1990).

Applicant contends that Ostermann never shows that PAF degradation correlates with reduced level of PAF and never addressed anti-PAF antibodies. This argument was carefully considered but not found persuasive because a reference is not overcome by pointing out that a reference lacks a teaching for which other references are relied. *In re Lyons*, 364 F.2d 1005, 150 USPQ 741, 746 (CCPA 1966).

Specifically Muzya et al. teach the detection of anti-PAF antibodies. While Ostermann et al. teach that the mean PAF-degrading capacity of serum from myocardial infarction survivors were found to be significantly increased in comparison to control serum samples. See page 533

last two paragraphs. PAF is further taught to play a role in the development of atherosclerosis. See page 536 discussion, for example.

Applicant's arguments against the reference of Baldo et al. are MOOT because the reference has been removed/withdrawn.

9. For reasons aforementioned, no claims are allowed.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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